

Impact of expert centers annual case volume on outcomes of minimally-invasive liver resections: international multicenter study

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Background: Presently, evidence on the volume-outcome relationship for minimally-invasive liver resections (MILR) remains heterogeneous. This study aimed to investigate the volume-outcome relationships in expert centers which had already mounted the initial learning curve of MILR and had a case

volume of >20 MILR/annum.

Methods: This was an international multicenter retrospective analysis of 22,210 patients undergoing MILR between 2015 and 2022 at 64 centers. Centers were stratified into medium volume (MV), high volume (HV) and very high volume (VHV) defined as 20–50/51–80 and >80 MLR/annum. Difficulty of resections was graded according to the Iwate score and Institute Mutualiste Montsouris (IMM) system.

Results: A total of 19,691 MILR met study criteria and were included. Of the 19,961 patients, 4,747 (25.6%), 4,222 (23.8%) and 10,243 (50.7%) were performed in 28 MV, 15 HV and 17 VHV centers, respectively. In the overall IMM I and IMM III cohorts, open conversion rates were consistently significantly higher in MV centers. Significantly, in the subgroup analysis of IMM 3 MILR, the VHV cohort had less blood loss [>500 mL: 443.7 (19.6%) *vs.* 221.6 (22.1%) (MV) *vs.* 296.9 (26.0%) (HV), $P=0.001$], shorter operative times [292 *vs.* 362.7 (MV) *vs.* 372.9 (HV) min, $P<0.001$] and shorter postoperative stay [7.8 *vs.* 8.3 (MV) and 10 (HV) days, $P<0.001$]. However, the HV cohort had the lower rates of open conversion [79.4 (7.0%) *vs.* 174.3 (7.7%) (VHV) *vs.* 103.2 (10.3%) (MV); $P=0.03$].

Conclusions: Center volume-outcome relationship beyond 20 MILR/annum was not clear and results were heterogenous suggesting that factors other than center volume alone had a more significant impact on perioperative outcomes of MILR in these expert centers.

Keywords: Minimally-invasive liver resections (MILRs); volume; outcome; high volume (HV); laparoscopic liver resection (laparoscopic LR)

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Introduction

The impact of hospital volume on peri-operative outcomes of complex surgical procedures has been a subject of debate over the past two decades (1,2). The volume-outcome relationship for procedures such as esophagectomy or pancreatic surgery has been shown to be associated with superior outcomes in high volume (HV) compared to low volume (LV) centers (3,4). Evidence on the volume-outcome relationship for liver resections (LRs) remains heterogeneous. While strong associations between center volume and peri-operative outcomes were reported in French (5) and German (6) studies, a similar result was not found in a Dutch study (2).

Despite technological advancements and accumulating surgeon experience in minimally-invasive liver resections (MILRs) (7-9), most consensus guidelines today recommend that MILR still only be performed in HV centers with sub-specialty expertise in both minimally invasive and hepatobiliary surgery (10,11). Three recently published large European studies reported significant volume-outcome relationships for MILR (12-14). An Italian study, which classified HV centers as those performing >2 MILR/month, found that the strongest volume-outcome relationships were for complex MILR (major hepatectomies

or posterosuperior resections) (12). In a French study, investigators reported volume cutoffs of 25 MILR per year and 35 MILR per year as being significantly associated with achievement of benchmark outcomes after minor (left lateral sectionectomies) and major (right hepatectomies) MILR, respectively (13). In a Dutch study, investigators reported that centers performing >20 MILR per year were associated with better outcomes, in particular for patients undergoing major hepatectomies (14). A common major confounding factor of these studies was that the MILR was performed before the learning curve had been surmounted.

Presently, it remains unknown if the volume-outcome relationship persists beyond this annual case volume in expert centers (performing more than 20 cases/annum). Some studies have suggested that HV liver centers be defined as those performing >50 or even beyond 80 cases per annum (2,15). Hence, this study aimed to investigate the volume-outcome relationships in expert centers that had mounted the initial learning curve of MILR and had a case volume of >20 MILR/annum. We present this article in accordance with the STROBE reporting checklist (available at <https://hbsn.amegroups.com/article/view/10.21037/hbsn-2024-666/rc>).

Methods

This is an international multicenter retrospective analysis of patients who underwent MILR between 2015 and 2022 at 64 centers. All institutions obtained their respective approvals according to their local requirements. This study was approved by the Singapore General Hospital Institution Review Board (2020/2802) and the need for any further board review and patient consent was waived. All anonymized data were collated and analyzed centrally at the Singapore General Hospital. The study was performed in accordance with the Declaration of Helsinki and its subsequent amendments.

MILR was defined as pure laparoscopic and robotic-assisted laparoscopic LR. Hand-assisted laparoscopic and laparoscopic-assisted (hybrid) resections (defined as cases whereby mobilization was performed via laparoscopy and parenchymal transection was performed via an open incision) were both excluded. LR with concomitant bilio-anastomosis, associating liver partition and portal vein

ligation for staged hepatectomy and donor hepatectomies for liver transplant, were also excluded. The confounding effect caused by operators during their initial learning curve was reduced by including only cases performed after 2015. To further minimize this effect, only centers with a cumulative experience of at least 50 MILR (16) and performing an average of at least 20 MILR per year (14) during the study period of 2015–2022 were included. This was based on a recent systematic review on learning curves in L-LR, which reported that 50 cases were needed to mount the learning curve (16).

Comparative analyses of perioperative outcomes of MILR performed at expert liver centers with different annual case volume was carried out before and after inverse probability weighting adjustment for confounding baseline clinicopathological factors. Additional subset analyses were performed for hepatectomies of varying difficulty levels.

Definitions

Resections were classified according to the 2000 Brisbane nomenclature (17). Post-operative complications were graded according to the Clavien-Dindo classification and recorded for up to 30 days or during the same hospitalisation (18). The centers were arbitrarily classified into medium volume (MV) group (20–50 cases per year), HV group (51–80 cases per year) and very high volume (VHV) group (>80 cases per year). Difficulty of resections was graded according to the Iwate score (9) and Institute Mutualiste Montsouris (IMM) classification system (19,20).

Statistical analysis

To minimize confounding and selection biases, a doubly inverse probability of treatment weighting (IPTW) was performed using propensity scores conditioned on covariates including age, sex, year, geographical region, American Society of Anesthesiologists (ASA) score, laparoscopic/robotic, previous abdominal surgery, previous liver surgery, malignant pathology, pathology type, cirrhosis, severity of cirrhosis, portal hypertension, tumor size, tumor multifocality, multiple resections, tumor location, major LR and concomitant other operative procedure (21–25). As the exposure variable is multivalued (annual center volume was stratified into three categories) and there may exist nonlinear relationships or interactions between propensity-score covariates, a generalised boosted model (GBM) using the adaptive boosting (AdaBoost) machine learning

Highlight box

Key findings

- Center volume–outcome relationship beyond 20 minimally-invasive liver resections (MILRs)/annum in experienced centers was not clear and results were heterogeneous suggesting that factors other than center volume alone had a more significant impact on perioperative outcomes of MILR in these expert centers.

What is known and what is new?

- Evidence on the volume–outcome relationship for liver resections (LRs) remains heterogeneous. While strong associations between center volume and peri-operative outcomes were reported in some studies, especially with regard to low versus high volume centers, other studies did not demonstrate such an association.
- This is the first study to study the volume–outcome relationships in expert centers that had already mounted the initial learning curve of MILRs and had a case volume of >20 MILR/annum. It demonstrated that center volume–outcome relationship beyond 20 MILR/annum in experienced centers was not clear. The results in this study were heterogeneous suggesting that factors other than center volume alone had a more significant impact on perioperative outcomes of MILR in these expert centers.

What is the implication, and what should change now?

- In this study, the volume–outcome relationship beyond 20 cases/annum was not clear, suggesting that factors other than center volume alone could have a more significant impact on perioperative outcomes of MILR in these expert centers. These findings may guide countries in deciding to implement centralisation of some surgical procedures, balancing travel time and equality of healthcare access.

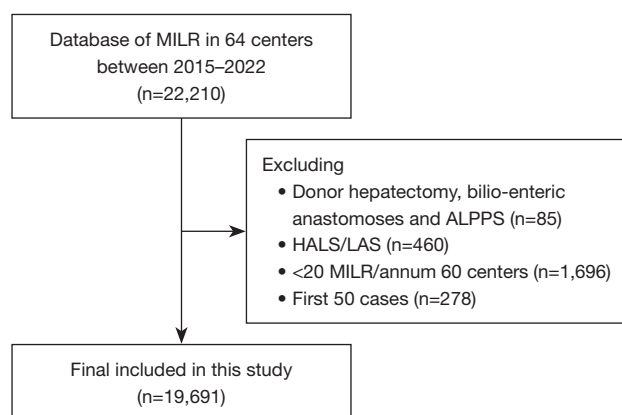


Figure 1 PRISMA diagram showing selection of study cohort. ALPPS, associating liver partition and portal vein ligation for staged hepatectomy; HALS, hand-assisted laparoscopic surgery; LAS, laparoscopic assisted surgery; MILR, minimally-invasive liver resection.

ensemble algorithm was fitted to estimate the probability of exposure assignment (26,27). Propensity-scores were trimmed at a delta of 0.1 to reduce the impact of extreme propensity-scores and improve the finite-sample property of IPTW. Statistical analyses were conducted in R version 4.2.3, and nominal $P < 0.05$ were considered statistically significant.

Results

A total of 22,210 patients were reviewed, of which 19,691 patients undergoing MILR at 60 international centers met the study final criteria: 5,016 MILR (25.6%) were performed in 28 MV centers, 4,693 MILR (23.8%) in 15 HV centers and 9,982 MILR (50.7%) in 17 VHV centers. *Figure 1* summarises the selection of patients in this study. After IPTW, baseline covariates were well-balanced (*Figures S1-S4*, and *Tables 1-4*).

Overall cohort

In the entire unweighted cohort (19,212 patients), the 3 groups had significant differences in terms of many baseline clinicopathological parameters as shown in *Table 1*. After IPTW, all clinicopathological differences were adjusted. The comparison of MV *vs.* HV *vs.* VHV groups in terms of perioperative outcomes was summarised in *Table 2*.

After IPTW (*Table 2*), open conversion rates were highest for MV centers and operative times were shortest for VHV

centers. MILR in HV centers had significantly increased rates of considerable blood loss but were also associated with a less frequent application of the Pringle maneuver. In contrast, higher intraoperative blood transfusion rates and shorter Pringle times were recorded in the VHV group. Regarding postoperative outcomes, it was noted that patients in HV centers had longer postoperative stay with lower readmission and lower major morbidity rates. In addition, a lower number of patients in MV centres had close/involved margins for malignancy.

Subset analysis in IMM I patients

In the subgroup of patients undergoing MILR of low difficulty (IMM grade I, 10,479 patients), there were no significant differences in baseline clinicopathological characteristics after IPTW (*Table S1*). The comparison of MV *vs.* HV *vs.* VHV groups in terms of perioperative outcomes was summarised in *Table S2*.

After IPTW, conversion rates were higher for MV centers and operative times shorter for VHV centers. There was less frequent application of the Pringle maneuver for HV centers and higher intraoperative blood transfusion rates for VHV centres. Pringles timings were significantly shorter in the VHV group. With regards to post-operative outcomes, patients in HV centres had longer postoperative and higher readmission rates. There was a higher rate of major morbidity for VHV centers. Patients with malignant diseases who were operated on in MV centres had a lower frequency of close/involved margins

Subset analysis of IMM III patients

In the subgroup of patients undergoing MILR of great difficulty (IMM grade III, 4,815 patients), there were no significant differences in baseline clinicopathological characteristics after IPTW (*Table 3*). The comparison between MV *vs.* HV *vs.* VHV groups in terms of perioperative outcomes was summarised in *Table 4*.

After IPTW, open conversion rates were significantly higher for MV centers and operative times shorter for VHV centers. The frequency of MILR with considerable blood loss (>500 mL) was lower for VHV centers, despite higher intra-operative blood transfusion rates. VHV centers used Pringles maneuver more frequently but with an overall shorter duration of Pringles time as compared to MV and HV centers. Regarding postoperative outcomes, patients from VHV centers had shorter postoperative stays

Table 1 Comparison between baseline clinicopathological characteristics of MILR by center volume

Baseline characteristics	Unweighted cohort				Inverse probability of treatment weighted cohort			
	MV (n=4,747)	HV (n=4,222)	VHV (n=10,243)	P value	MV (n=4,747)	HV (n=4,222)	VHV (n=10,243)	P value
Age, years	62.6±13.1	62.7±13.8	58.9±13.5	<0.001	62.2±13.3	62.1±13.4	62.1±13.3	0.92
Male sex	2,896 (61.0)	1,747 (58.6)	6,702 (65.4)	<0.001	2,899.5 (61.1)	2,553.4 (60.5)	6,269.5 (38.8)	0.77
Year				<0.001				0.21
2015–2016	1,120 (23.6)	980 (23.2)	1,774 (17.3)		1,085.8 (22.9)	957.6 (22.7)	2,253.7 (22.0)	
2017–2019	2,312 (48.7)	2,280 (54.0)	5,826 (56.9)		2,552.6 (53.8)	2,367.0 (56.1)	5,845.2 (57.1)	
2020–2021	1,315 (27.7)	962 (22.8)	2,643 (25.8)		1,108.6 (23.4)	897.3 (21.3)	2,144.1 (20.9)	
Geographical region				<0.001				0.13
East	1,442 (30.4)	1,139 (27.0)	7,670 (74.9)		1,945.0 (41.0)	1,731.7 (41.0)	4,613.6 (45.0)	
West	3,305 (69.6)	3,083 (73.0)	2,573 (25.1)		2,802.0 (59.0)	2,490.3 (59.0)	5,629.4 (55.0)	
ASA score				<0.001				0.23
I/II	2,773 (58.4)	3,101 (73.4)	8,462 (82.6)		3,300.5 (69.5)	3,059.0 (72.5)	7,269.8 (71.0)	
III/IV	1,974 (41.6)	1,121 (26.6)	1,781 (17.4)		1,446.5 (30.5)	1,162.5 (27.5)	2,973.2 (29.0)	
MILR type				<0.001				0.14
Pure laparoscopic	3,721 (78.4)	3,787 (89.7)	8,817 (86.1)		4,116.8 (86.7)	3,729.7 (88.3)	8,964.2 (87.5)	
Robotic-assisted laparoscopic	1,026 (21.6)	435 (10.3)	1,426 (13.9)		630.2 (13.3)	492.3 (11.7)	1,278.8 (12.5)	
Previous abdominal surgery	2,091 (44.0)	2,036 (48.2)	3,454 (33.7)	<0.001	1,984.4 (41.8)	1,817.7 (43.1)	4,505.9 (44.0)	0.49
Previous liver surgery	339 (7.1)	539 (12.8)	903 (8.8)	<0.001	396.2 (8.3)	434.9 (10.3)	1,066.6 (10.4)	0.1
Malignant pathology	4,011 (84.5)	3,493 (82.7)	8,407 (82.1)	0.001	3,999.7 (84.3)	3,518.4 (83.3)	8,646.7 (84.4)	0.35
Pathology type				<0.001				0.71
HCC/ICC	2,141 (45.1)	1,508 (35.7)	5,865 (57.3)		2,162.0 (45.5)	1,848.5 (43.8)	4,639.4 (45.3)	
CRM/other metastases	1,791 (37.7)	1,886 (44.7)	2,419 (23.6)		1,768.0 (37.2)	1,599.3 (37.9)	3,850.7 (37.6)	
Other malignancy	79 (1.7)	96 (2.3)	120 (1.2)		69.7 (1.5)	68.7 (1.6)	154.1 (1.5)	
Benign	736 (15.5)	732 (17.3)	1,839 (18.0)		747.3 (15.7)	705.6 (16.7)	1,598.8 (15.6)	
Cirrhosis	1,344 (28.3)	932 (22.1)	3,478 (34.0)	<0.001	1,328.0 (28.0)	1,064.2 (25.2)	2,773.5 (27.1)	0.24
Child-Pugh score				<0.001				0.1
No cirrhosis	3,404 (71.7)	3,290 (77.9)	6,766 (66.1)		3,419.6 (72.0)	3,157.8 (74.8)	7,469.9 (72.9)	
A	1,291 (27.2)	869 (20.6)	3,026 (29.5)		1,268.9 (26.7)	993.5 (23.5)	2,544.6 (24.8)	
B	52 (1.1)	63 (1.5)	451 (4.4)		58.5 (1.2)	70.7 (1.7)	228.4 (2.2)	
Portal hypertension	289 (6.1)	372 (8.8)	832 (8.1)	<0.001	297.6 (6.3)	325.6 (7.2)	684.3 (6.7)	0.45
Tumour size, mm	34.2±26.3	35.2±28.2	40.7±31.1	<0.001	35.6±27.6	26.4±28.1	36.6±28.7	0.35
Multifocal	1,019 (21.5)	1,222 (28.9)	1,988 (19.4)	<0.001	1,080.1 (22.8)	1,027.0 (24.3)	2,484.6 (24.3)	0.18
Multiple resections	541 (11.4)	707 (16.7)	1,074 (10.5)	<0.001	601.8 (12.7)	567.6 (13.4)	1,465.6 (14.3)	0.46

Table 1 (continued)

Table 1 (continued)

Baseline characteristics	Unweighted cohort				Inverse probability of treatment weighted cohort			
	MV (n=4,747)	HV (n=4,222)	VHV (n=10,243)	P value	MV (n=4,747)	HV (n=4,222)	VHV (n=10,243)	P value
Posterosuperior segments	1,929 (40.6)	2,039 (48.3)	4,796 (46.6)	<0.001	2,066.2 (43.5)	1,880.9 (44.6)	4,520.9 (44.1)	0.68
Major resections (3 segments)	739 (15.6)	717 (17.0)	1,826 (17.8)	0.003	799.6 (16.8)	749.9 (17.8)	1,763.2 (17.2)	0.41
Concomitant other operative procedure (non-cholecystectomy)	709 (14.9)	656 (15.5)	1,538 (15.0)	0.67	703.1 (14.8)	594.0 (14.1)	1,575.7 (15.4)	0.19
IMM difficulty				<0.001				0.12
Grade I	2,792 (58.8)	2,240 (53.1)	5,447 (53.2)		2,624.7 (55.3)	2,304.6 (54.6)	5,748.4 (56.1)	
Grade II	950 (20.0)	841 (19.9)	2,127 (20.8)		1,012.1 (21.3)	853.6 (20.2)	2,000.3 (19.5)	
Grade III	1,005 (21.2)	1,141 (27.0)	2,669 (26.1)		1,110.2 (23.4)	1,063.8 (25.2)	2,494.3 (24.4)	
IMM procedure type (19)				<0.001				0.69
Wedge anterolateral	1,339 (28.2)	1,010 (23.9)	2,155 (21.0)		1,182.0 (24.9)	1,040.9 (24.7)	2,564.0 (25.0)	
Wedge posterosuperior	753 (15.9)	786 (18.6)	1,883 (18.4)		804.8 (17.0)	720.0 (17.1)	1,867.6 (18.2)	
Left lateral sectionectomy	700 (14.7)	444 (10.5)	1,409 (13.8)		637.9 (13.4)	543.7 (12.9)	1,316.8 (12.9)	
Segmentectomy anterolateral	605 (12.7)	582 (13.8)	1,279 (12.5)		642.3 (13.5)	545.1 (12.9)	1,269.8 (12.4)	
Left hepatectomy	345 (7.3)	259 (6.1)	848 (8.3)		369.8 (7.8)	308.5 (7.3)	730.5 (7.1)	
Segmentectomy posterosuperior	332 (7.0)	427 (10.1)	917 (9.0)		384.4 (8.1)	363.9 (8.6)	866.6 (8.5)	
Right hepatectomy	301 (6.3)	354 (8.4)	716 (7.0)		341.9 (7.2)	340.8 (8.1)	783.9 (7.7)	
Extended right hepatectomy	22 (0.5)	39 (0.9)	65 (0.6)		23.7 (0.5)	35.1 (0.8)	82.3 (0.8)	
Right posterior sectionectomy	211 (4.4)	185 (4.4)	542 (5.3)		207.6 (4.4)	188.8 (4.5)	443.3 (4.3)	
Right anterior/central hepatectomy	100 (2.1)	102 (2.4)	368 (3.6)		120.0 (2.5)	100.4 (2.4)	259.1 (2.5)	
Extended left hepatectomy	39 (0.8)	34 (0.8)	61 (0.6)		32.5 (0.7)	34.7 (0.8)	59.1 (0.6)	
Iwate score (9)				<0.001				0.94
Low	1,112 (23.4)	856 (20.3)	1,639 (16.0)		996.1 (21.0)	881.5 (20.9)	2,087.1 (20.4)	
Intermediate	1,993 (42.0)	1,713 (40.6)	4,310 (42.1)		1,947.9 (41.0)	1,728.1 (40.9)	4,290.5 (41.9)	
High	990 (20.9)	980 (23.2)	2,553 (24.9)		1,075.9 (22.7)	955.9 (22.6)	2,326.1 (22.7)	
Expert	652 (13.7)	673 (15.9)	1,741 (17.0)		727.1 (15.3)	656.6 (15.6)	1,539.4 (15.0)	

Data are presented as mean $\pm$ standard deviation or n (%). ASA, American Society of Anesthesiologists; CRM, colorectal metastasis; HCC, hepatocellular carcinoma; HV, high volume; ICC, intrahepatic cholangiocarcinoma; IMM, Institute Mutualiste Montsouris; MILR, minimally-invasive liver resection; MV, medium volume; VHV, very high volume.

Table 2 Comparison between perioperative outcomes stratified by center volume

Perioperative outcomes	Unweighted cohort				Inverse probability of treatment weighted cohort			
	MV (n=4,747)	HV (n=4,222)	VHV (n=10,243)	P value	MV (n=4,747)	HV (n=4,222)	VHV (n=10,243)	P value
Operating time, min	250.6±126.1	264.3±153.2	214.84±112.1	<0.001	257.7±128.0	268.8±163.6	215.4±113.1	<0.001
Blood loss, mL	247.7±431.4	254.8±424.9	255.3±386.1	0.61	257.0±449.6	265.9±471.6	260.7±381.2	0.75
Blood loss (categories), mL				0.03				0.006
<500	4,284 (90.2)	3,739 (88.6)	9,190 (89.7)		4,235.0 (89.2)	3,706.3 (87.8)	9,210.4 (89.9)	
≥500	463 (9.8)	483 (11.4)	1,053 (10.3)		511.8 (10.8)	515.7 (12.2)	1,032.6 (10.1)	
No intraoperative blood transfusion	4,516 (95.3)	4,016 (95.3)	9,301 (91.1)	<0.001	4,501.3 (94.9)	3,997.8 (94.8)	9,236.8 (90.8)	<0.001
Pringle maneuver applied	2,350 (50.1)	1,814 (43.1)	5,862 (59.1)	<0.001	2,521.2 (53.9)	1,671.7 (39.7)	4,948.7 (50.2)	<0.001
Pringle duration applied, min	55.4±38.6	51.9±38.8	40.4±26.5	<0.001	58.4±39.1	55.2±41.6	39.3±25.4	<0.001
Open conversion	315 (6.6)	177 (4.2)	509 (5.0)	<0.001	323.9 (6.8)	152.1 (3.6)	595.8 (5.8)	<0.001
Postoperative stay, days	5.9±5.2	7.2±8.5	6.8±5.7	<0.001	6.3±5.5	7.6±9.0	6.3±6.1	<0.001
30-day readmission	178 (3.8)	127 (3.0)	327 (3.2)	0.10	168.1 (3.5)	128.6 (3.0)	431.7 (4.2)	0.01
Postoperative morbidity	921 (19.4)	795 (18.8)	1,684 (16.4)	<0.001	915.7 (19.3)	738.1 (17.5)	1,889.5 (18.5)	0.16
Major morbidity (Clavien-Dindo >2) (18)	310 (6.5)	243 (5.8)	502 (4.9)	<0.001	304.9 (6.4)	233.7 (5.5)	701.4 (6.9)	0.04
Reoperation	76 (1.6)	55 (1.3)	109 (1.1)	0.021	76.5 (1.6)	52.3 (1.2)	177.5 (1.7)	0.18
30-day mortality	24 (0.5)	20 (0.5)	33 (0.3)	0.18	23.3 (0.5)	18.1 (0.4)	43.1 (0.4)	0.86
In-hospital mortality	28 (0.6)	23 (0.5)	39 (0.4)	0.16	26.5 (0.6)	22.7 (0.5)	46.7 (0.5)	0.73
90-day mortality	30 (0.6)	30 (0.7)	57 (0.6)	0.54	27.9 (0.6)	29.8 (0.7)	73.2 (0.7)	0.73
Close/involved margins (≤1 mm) for malignancies	729 (15.5)	885 (21.0)	1,684 (16.5)	<0.001	731.1 (15.5)	823.8 (19.6)	1,869.0 (18.4)	<0.001

Data are presented as mean ± standard deviation or n (%). HV, high volume; MV, medium volume; VHV, very high volume.

compared to HV and MV centers.

Discussion

This study aimed to investigate volume-outcome relationships in a large international database of MILR performed in MV, HV and VHV expert centers defined as centers that have mounted the early learning curve of 50 cases and perform an average of 20 MILR cases per annum. The results suggested that the volume-outcome relationship was less apparent in these expert centers, unlike the previous study (15), and the results were mixed as there was no clear trend demonstrating superior outcomes with higher volume centers in this study cohort.

One of the main significant findings in this analysis was that MILR performed in MV centers was associated

with a higher open conversion rate compared to HV and VHV in the overall cohort. This finding was also observed in both the IMM I and III subset analyses. Of note, HV centers seemed to be associated with the lowest rate of open conversion and this was also observed in the subset analyses of IMM I and III cases. The abovementioned findings on open conversion rates suggested a significant impact of hospital volume on the technical success and feasibility of MILR exists even in centers performing over 20 cases/annum but not beyond 50 cases/annum. It also suggests that other factors, such as case selection and the number of surgeons in a center (individual surgeon experience), may have an impact on open conversion rates.

The other findings in this study did not demonstrate a clear volume-outcome relationship. In the overall cohort, MV centers were associated with the lowest rate of blood

Table 3 Comparison between baseline clinicopathological characteristics of MILR in IMM grade III cases

Baseline characteristics	Unweighted cohort				Inverse probability of treatment weighted cohort			
	MV (n=1,005)	HV (n=1,141)	VHV (n=2,669)	P value	MV (n=1,005)	HV (n=1,141)	VHV (n=2,669)	P value
Age, years	62.5±12.6	63.4±13.7	58.2±13.5	<0.001	62.5±12.8	62.1±13.3	62.1±13.2	0.77
Male sex	654 (65.1)	699 (61.3)	1,789 (67.0)	0.003	655.6 (65.2)	723.8 (63.4)	1,830.2 (68.6)	0.56
Year				<0.001				0.43
2015–2016	199 (19.8)	256 (22.4)	432 (16.2)		200.5 (19.9)	224.9 (19.7)	453.4 (20.0)	
2017–2019	502 (50.0)	606 (53.1)	1,534 (57.5)		542.1 (53.9)	642.7 (56.3)	1,300.8 (57.3)	
2020–2021	304 (30.2)	279 (24.5)	703 (26.3)		262.4 (26.1)	273.4 (24.0)	514.8 (22.7)	
Geographical region				<0.001				0.1
East	319 (31.7)	356 (31.2)	2,085 (78.1)		441.7 (43.9)	513.9 (45.0)	1,547.3 (58.0)	
West	686 (68.3)	785 (68.8)	584 (21.9)		563.3 (56.1)	627.1 (55.0)	1,121.7 (42.0)	
ASA score				<0.001				0.32
I/II	528 (52.5)	847 (74.2)	2,211 (82.8)		691.1 (68.8)	817.6 (71.7)	2,023.3 (75.8)	
III/IV	477 (47.5)	294 (25.8)	458 (17.2)		313.9 (31.2)	323.4 (28.3)	645.7 (24.2)	
MILR type				<0.001				0.56
Pure laparoscopic	750 (74.6)	1,004 (88.0)	2,231 (83.6)		852.9 (84.9)	986.7 (86.5)	2,356.1 (86.2)	
Robotic-assisted	255 (25.4)	137 (12.0)	438 (16.4)		152.1 (15.1)	154.3 (13.5)	312.9 (13.8)	
Previous abdominal surgery	445 (44.3)	521 (45.7)	802 (30.0)	<0.001	406.5 (40.4)	439.9 (38.6)	916.4 (40.4)	0.62
Previous liver surgery	72 (7.2)	155 (13.6)	185 (6.9)	<0.001	73.1 (7.3)	107.2 (9.4)	203.7 (9.0)	0.24
Malignant pathology	891 (88.7)	1,011 (88.6)	2,290 (85.8)	0.02	899.1 (89.5)	1,005.7 (88.1)	2,028.4 (89.4)	0.55
Pathology type				<0.001				0.8
HCC/ICC	498 (49.6)	446 (39.1)	1,733 (64.9)		507.8 (50.5)	573.1 (50.2)	1,186.5 (52.3)	
CRM/other metastases	383 (38.1)	547 (47.9)	525 (19.7)		379.3 (37.7)	416.8 (36.5)	805.3 (35.5)	
Other malignancy	10 (1.0)	18 (1.6)	31 (1.2)		12.1 (1.2)	15.8 (1.4)	36.4 (1.6)	
Benign	114 (11.3)	130 (11.4)	380 (14.2)		105.9 (10.5)	135.3 (11.9)	240.9 (10.6)	
Cirrhosis	261 (26.0)	231 (20.2)	953 (35.7)	<0.001	282.7 (28.1)	282.6 (24.8)	630.6 (27.8)	0.2
Child-Pugh score				<0.001				0.11
No cirrhosis	744 (74.0)	910 (79.8)	1,716 (64.3)		722.3 (71.9)	858.4 (75.2)	1,638.4 (72.2)	
A	257 (25.6)	219 (19.2)	826 (30.9)		278.6 (27.7)	269.3 (23.6)	586.7 (25.9)	
B	4 (0.4)	12 (1.1)	127 (4.8)		4.1 (0.4)	13.2 (1.2)	43.9 (1.9)	
Portal hypertension	37 (3.7)	69 (6.0)	180 (6.7)	0.002	44.2 (4.4)	66.2 (5.8)	116.2 (5.1)	0.42
Tumor size, mm	44.1±30.5	43.1±30.3	51.2±35.6	<0.001	44.9±31.6	46.1±31.6	46.3±32.2	0.52
Multifocal	269 (26.8)	413 (36.2)	593 (22.2)	<0.001	275.0 (27.4)	334.3 (29.3)	659.8 (29.1)	0.62
Multiple resections	99 (9.9)	151 (13.2)	203 (7.6)	<0.001	105.8 (10.5)	110.5 (9.7)	253.5 (11.2)	0.51
Posterosuperior segments	932 (92.7)	1,072 (94.0)	2,422 (90.7)	0.002	926.1 (92.1)	1,049.5 (92.0)	2,070.0 (91.3)	0.71
Major resection (3 segments)	612 (60.9)	684 (59.9)	1,698 (63.6)	0.07	613.8 (61.1)	669.9 (58.7)	1,344.4 (59.2)	0.59

Table 3 (continued)

Table 3 (continued)

Baseline characteristics	Unweighted cohort				Inverse probability of treatment weighted cohort			
	MV (n=1,005)	HV (n=1,141)	VHV (n=2,669)	P value	MV (n=1,005)	HV (n=1,141)	VHV (n=2,669)	P value
Concomitant other operative procedure (non-cholecystectomy)	124 (12.3)	113 (9.9)	331 (12.4)	0.08	120.1 (11.9)	114.8 (10.1)	261.8 (11.5)	0.39
Procedure type (19)				<0.001				0.95
Segmentectomy posterosuperior	332 (33.0)	427 (37.4)	917 (34.4)		350.4 (43.9)	390.2 (34.2)	795.4 (35.1)	
Right/extended right hepatectomy	323 (32.2)	393 (34.4)	781 (29.2)		333.7 (33.2)	404.0 (35.4)	775.7 (34.2)	
Right posterior sectionectomy	211 (21.0)	185 (16.2)	542 (20.3)		184.9 (18.4)	202.9 (17.8)	398.7 (17.6)	
Central hepatectomy/right anterior/extended left hepatectomy	139 (13.9)	136 (11.9)	429 (16.1)		135.9 (13.5)	144.0 (12.6)	299.1 (13.1)	
Iwate score (9)				<0.001				0.49
Low	0	0	0		0	0	0	
Intermediate	1 (0.1)	4 (0.4)	42 (1.6)		1.8 (0.2)	8.8 (0.8)	19.9 (0.9)	
High	423 (42.1)	521 (45.7)	1,096 (41.1)		425.7 (42.4)	492.2 (43.1)	961.2 (42.4)	
Expert	581 (57.8)	616 (54.0)	1,531 (57.4)		577.5 (57.5)	639.9 (56.1)	1,287.9 (56.8)	

Data are presented as mean $\pm$ standard deviation or n (%). ASA, American Society of Anesthesiologists; CRM, colorectal metastasis; HCC, hepatocellular carcinoma; HV, high volume; ICC, intrahepatic cholangiocarcinoma; IMM, Institute Mutualiste Montsouris; MILR, minimally-invasive liver resection; MV, medium volume; VHV, very high volume.

transfusion, shortest postoperative stay and lowest rate of close/involved resection margins. HV centers, on the other hand, were associated with the lowest rate of 30-day readmission and major morbidity, whereas VHV centers were associated with the shortest operation time and lowest rate of major blood loss ≥ 500 mL. While Pringles maneuver was used least frequently in HV centers, the duration of application was shortest in VHV centers.

Potential important confounders in this study to highlight include blood transfusion rates, which may be related to individual centers' transfusion protocols, whereas length of stay would be influenced by enhanced recovery after surgery (ERAS) protocols and geographical location of centers, which are heavily influenced by geographical variations in national medical reimbursement policies. Operation time may also be influenced by surgical practices and technique such as the use of precise anatomical LR versus non-anatomical resections or the use of staplers versus ultrasonic devices to transect the liver parenchyma.

In the subset analyses of IMM III procedures, VHV centers were associated with reduced operative times, lower

rates of blood loss ≥ 500 mL and shorter post-operative stays. MV centers required the least intraoperative blood transfusions but made use of the Pringles maneuver most frequently. VHV centers had the shortest average duration of Pringles time, while HV centers had the lowest rates of open conversion. These findings may possibly be attributed to the multidisciplinary experience in larger centers, which could contribute positively to improved perioperative management and outcomes.

Contrary to the present findings, a significant volume-outcome relationship for MILR had been recently reported in several European nation-wide studies (12–14). However, notably, these studies compared LV centers (performing <20–25 cases/annum) with HV centers. Furthermore, their results could be confounded by the inclusion of MILR cases performed during the pioneering phase, where the learning curve of early adopters had not been surmounted.

An important factor that could play a role in volume outcome relationships is the degree of technical difficulty. Vastly differing learning curves for hepatectomies of varying difficulties have been well reported in the literature

Table 4 Comparison between perioperative outcomes in grade III cases stratified by center volume

Perioperative outcomes	Unweighted cohort				Inverse probability of treatment weighted cohort			
	MV (n=1,005)	HV (n=1,141)	VHV (n=2,669)	P value	MV (n=1,005)	HV (n=1,141)	VHV (n=2,669)	P value
Operating time, min	360.1±129.6	354.0±166.6	290.0±113.4	<0.001	362.7±129.4	372.9±176.9	292.4±111.2	<0.001
Blood loss, mL	456.1±712.6	438.0±586.3	408.2±425.3	0.09	454.1±736.1	471.3±652.6	417.9±512.9	0.10
Blood loss (categories), mL				0.006				0.001
<500	782 (77.8)	868 (76.1)	2,148 (80.5)		783.4 (77.9)	844.1 (74.0)	2,225.3 (83.4)	
≥500	223 (22.2)	273.0 (23.9)	521 (19.5)		221.6 (22.1)	296.9 (26.0)	443.7 (19.6)	
Intraoperative blood transfusion	112 (11.1)	116 (10.2)	420 (15.8)	<0.001	111.8 (11.1)	130.8 (11.5)	393.1 (17.4)	<0.001
Pringle maneuver applied	695 (70.2)	628 (55.2)	1,908 (74.2)	<0.001	727.4 (73.6)	595.2 (52.4)	1,454.2 (67.1)	<0.001
Pringle duration, min	75.4±42.8	63.8±47.6	50.3±30.1	<0.001	78.9±42.6	67.9±49.5	47.9±30.0	<0.001
Open conversion	105 (10.4)	88 (7.7)	177 (6.6)	0.001	103.2 (10.3)	79.4 (7.0)	174.3 (7.7)	0.03
Postoperative stay, days	7.6±7.3	9.4±12.0	8.0±6.6	<0.001	8.3±7.7	10.0±13.1	7.8±6.9	<0.001
30-day readmission	55 (5.5)	59 (5.2)	126 (4.7)	0.61	50.9 (5.1)	65.2 (5.7)	136.4 (6.0)	0.65
Postoperative morbidity	317 (31.5)	303 (26.6)	626 (23.5)	<0.001	307.9 (30.6)	301.2 (26.4)	607.5 (26.8)	0.10
Major morbidity (Clavien-Dindo >2) (18)	123 (12.2)	122 (10.7)	217 (8.1)	<0.001	117.9 (11.7)	127.0 (11.1)	259.8 (11.5)	0.93
Reoperation	29 (2.9)	24 (2.1)	42 (1.6)	0.04	29.3 (2.9)	25.2 (2.2)	60.7 (2.7)	0.68
30-day mortality	15 (1.5)	9 (0.8)	14 (0.5)	0.01	11.9 (1.2)	8.2 (0.7)	14.0 (0.6)	0.24
In-hospital mortality	18 (1.8)	12 (1.1)	18 (0.7)	0.01	14.5 (1.4)	12.6 (1.1)	17.6 (0.8)	0.25
90-day mortality	18 (1.8)	14 (1.2)	26 (1.0)	0.13	14.5 (1.4)	14.9 (1.3)	27.9 (1.2)	0.90
Close/involved margins (≤1 mm) for malignancies	206 (20.6)	277 (24.3)	448 (16.8)	<0.001	201.7 (20.1)	256.3 (22.5)	443.6 (19.7)	0.23

Data are presented as mean ± standard deviation or n (%). HV, high volume; MV, medium volume; VHV, very high volume.

to date (16,28-31). A German analysis for open major LR reported lower mortality rates in centers performing at least 44 hepatectomies annually (6). In the Italian study, the authors found that patients undergoing complex MILR (major hepatectomies/posterosuperior resections) had a markedly more significant volume-outcome relationship in terms of post-operative morbidity (12). Similarly, the Dutch study reported that centers performing less than 20 MILR per year had the worst outcomes in a subgroup analysis of patients undergoing major resections (14). Nonetheless, subset analyses of IMM III procedures in the present study reported mixed results with regards to the volume-outcome relationship.

A recent multicenter European analysis by Gorgec *et al.* (32) reported higher use of MILR, reduced rates of open conversion and shorter hospital stay at HV centers (>50 MILR per year) compared to 20 LV/MV Dutch

centers (≤50 MILR per year). Further subgroup analysis stratified findings according to the Southampton difficulty score (33), which additionally identified a lower morbidity rate for hepatectomies of increased complexity performed in HV centers. Notably, this study was not randomized and failed to make use of other pseudo-randomization methods [inverse probability weighting (IPW), propensity score matching, etc.] to mitigate selection biases (32).

A well-known important confounder of center volume is individual surgeon experience and volume. It has been demonstrated that even within HV centers, the MILR outcomes of individual surgeons may differ according to each individual's experience (28,29,34). Moreover, other factors related to the learning curve and technical proficiency with MILR such as when MILR was adopted, the number of surgeons performing MILR, the proportion of cases performed via MILR compared to the total number

of LR in the center and even the proficiency/experience of the surgeons with minimally-invasive surgery and with other minimally-invasive surgical procedures, would undoubtedly have an impact on the outcomes of MILR in a center regardless of its annual volume. The impact of individual surgeon experience deserves further analysis in future studies.

There were several limitations associated with the current study, which should be highlighted. As a retrospective study, it could be limited by information and selection bias. Information on the exact cumulative experience with MILR that each center had acquired was not available and could potentially be a significant confounding factor (35,36). The number of individual surgeons performing MILR at each institution was also not known. As highlighted previously, in addition to institutional cumulative experience, individual surgeon experience is a well-recognized determinant of MILR outcomes (28,29). Bias could also arise from a lack of cross-institutional homogeneity of surgical technique, patient selection criteria, anaesthetic methods and post-operative care protocols. It is also important to highlight that stratification of the study cohort to 3 rather than 2 groups may have resulted in blurring of any trends and also reduced the power of statistical tests, reducing their sensitivity.

Conclusions

This was the first study to analyse the volume-outcome relationships of MILR performed in expert centers with specific exclusion of cases performed during the pioneering learning periods. In this study, the volume-outcome relationship beyond 20 cases/annum was not clear, suggesting that factors other than center volume alone could have a more significant impact on perioperative outcomes of MILR in these expert centers. These findings may guide countries in deciding to implement centralisation of some surgical procedures, balancing travel time and equality of healthcare access.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://hbsn.amegroups.com/article/view/10.21037/hbsn-2024-666/rc>

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was performed in accordance with the Declaration of Helsinki and its subsequent amendments. This retrospective study on anonymized patient data was approved by the Singapore General Hospital Institution Review Board (2020/2802) and the need for any further board review and patient consent

was waived. All institutions obtained their respective approvals according to their local requirements.

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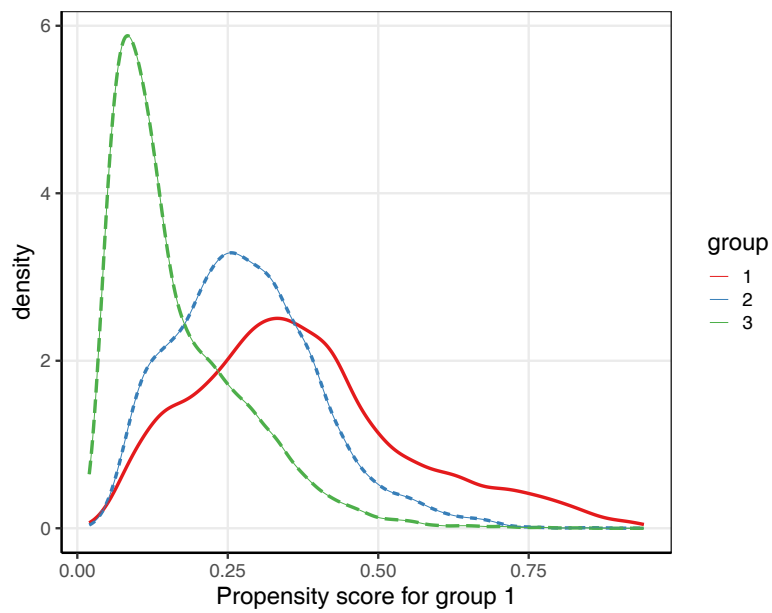


Figure S1 Propensity score distribution for MV centers.

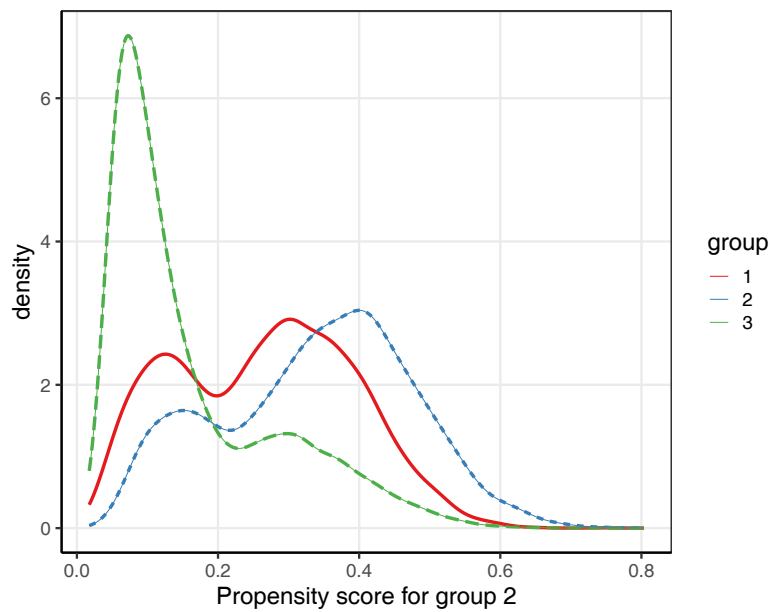


Figure S2 Propensity score distribution for HV centers.

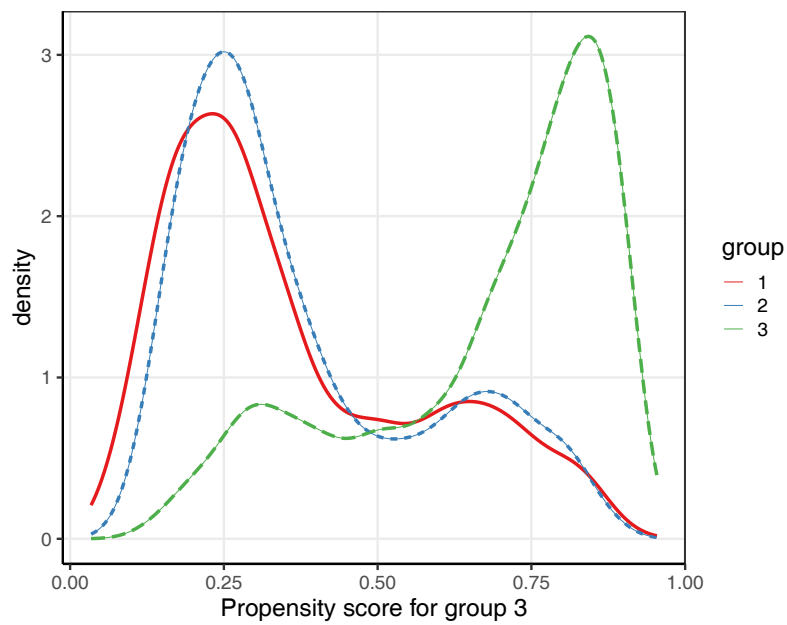


Figure S3 Propensity score distribution for VHV centers.

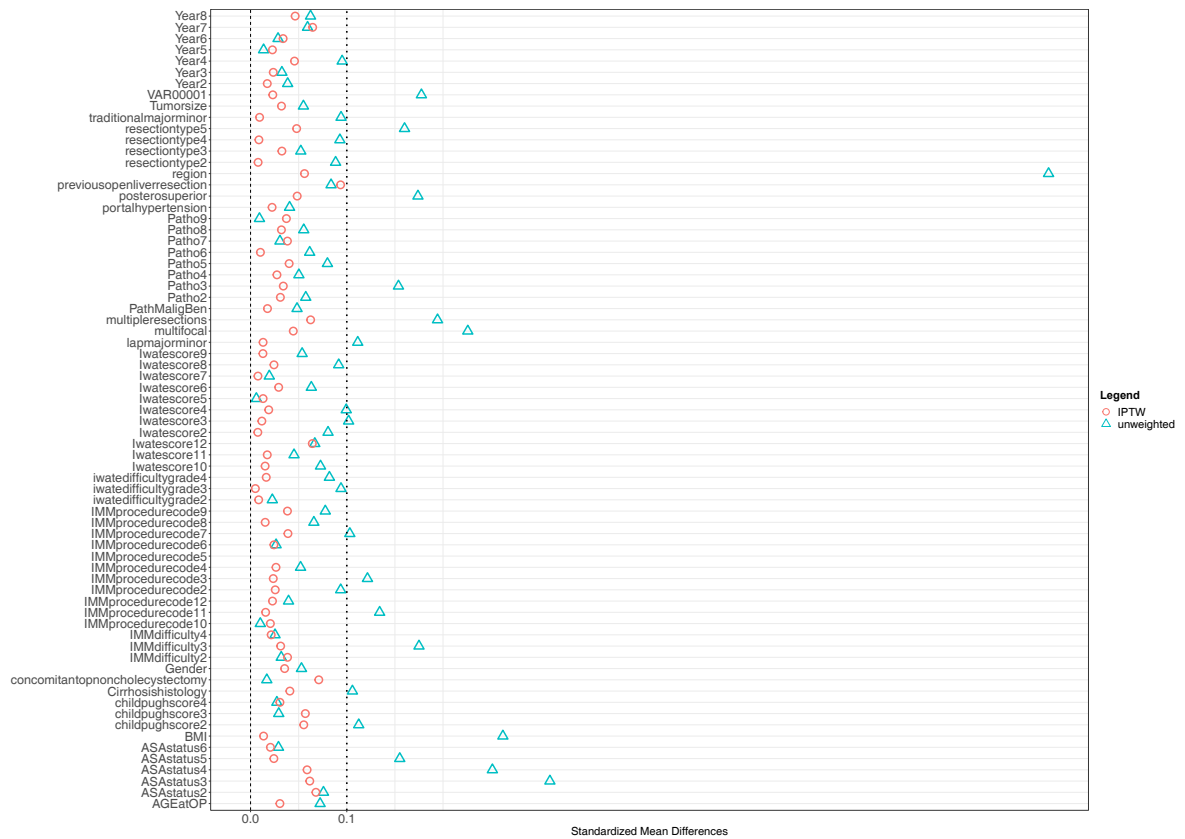


Figure S4 Love plots of propensity score distribution.

Table S1 Baseline characteristics of MILR in IMM grade 1

Baseline characteristics	Unweighted cohort				Inverse Probability of Treatment Weighted cohort			
	MV (n=2,792)	HV (n=2,240)	VHV (n=5,447)	P value	MV (n=2,792)	HV (n=2,240)	VHV (n=5,447)	P value
Age, years	62.4±13.4	61.9±13.9	59.5±13.5	<0.001	62.0±13.5	61.8±13.4	62.0±13.2	0.903
Male sex	1,667 (59.7)	1,289 (57.5)	3,545 (65.1)	<0.001	1,674.3 (60.0)	1,343.7 (60.0)	3,329.2 (61.1)	0.58
Year				<0.001				0.213
2015–2016	702 (25.1)	540 (24.1)	969 (27.8)		667.2 (23.9)	547.7 (24.5)	1,297.2 (23.8)	
2017–2019	1,326 (47.5)	1,219 (54.4)	3,012 (55.3)		1,491.1 (53.4)	1,237.0 (55.2)	3,063.1 (56.2)	
2020–2021	764 (27.4)	481 (21.5)	1,466 (26.9)		633.8 (22.7)	454.8 (20.3)	1,086.7 (19.9)	
Geographical region				<0.001				0.102
East	806 (28.9)	585 (26.1)	3,993 (73.3)		1,083.2 (38.8)	888.6 (39.7)	2,353.1 (43.2)	
West	1,986 (71.1)	1,655 (73.9)	1,454 (26.7)		1,708.8 (61.2)	1,351.4 (60.3)	3,093.9 (56.8)	
ASA score				<0.001				0.152
I/II	1,694 (60.7)	1,671 (74.6)	4,460 (81.9)		1,951.3 (69.9)	1,646.1 (73.5)	3,872.2 (71.1)	
III/IV	1,098 (39.3)	569 (25.4)	987 (18.1)		840.7 (30.1)	593.9 (26.5)	1,574.8 (28.9)	
MILR type				<0.001				0.297
Pure laparoscopic	2,241 (80.3)	2,080 (92.9)	4,767 (87.5)		2,477.4 (88.7)	2,036.2 (90.9)	4,864.1 (89.3)	
Robotic-assisted	551 (19.7)	160 (7.1)	680 (12.5)		314.6 (11.3)	203.8 (9.1)	582.9 (10.7)	
Previous abdominal surgery	1,258 (45.1)	1,128 (50.4)	2,019 (37.1)	<0.001	1,220.1 (43.7)	1,035.6 (46.2)	2,549.2 (46.8)	0.363
Previous liver surgery	217 (7.8)	320 (14.3)	545 (10.0)	<0.001	264.4 (9.5)	258.1 (11.5)	643.4 (11.8)	0.118
Malignant pathology	2,319 (83.1)	1,787 (79.8)	4,440 (81.5)	0.012	2,302.9 (82.5)	1,844.1 (82.3)	4,540.7 (83.4)	0.521
Pathology type				<0.001				0.843
HCC/ICC	1,152 (41.3)	690 (30.8)	2,834 (52.0)		1,135.3 (40.7)	871.6 (38.9)	2,205.8 (40.5)	
CRM/other metastases	1,124 (40.3)	1,064 (47.5)	1,539 (28.3)		1,137.2 (40.7)	945.3 (42.2)	2,267.2 (41.6)	
Other malignancies	43 (1.5)	31 (1.4)	65 (1.2)		30.4 (1.1)	25.7 (1.1)	65.8 (1.2)	
Benign	473 (16.9)	455 (20.3)	1,009 (18.5)		489.1 (17.5)	397.4 (17.7)	908.3 (16.7)	
Cirrhosis	824 (29.5)	494 (22.1)	1,791 (32.9)	<0.001	785.0 (28.1)	574.1 (25.6)	1,452.1 (26.7)	0.218
Childs Pugh score				<0.001				0.225
No cirrhosis	1,968 (70.5)	1,746 (77.9)	3,656 (67.1)		2,007.0 (71.9)	1,665.9 (74.4)	3,994.9 (73.3)	
A	785 (28.1)	457 (20.4)	1,573 (28.9)		742.4 (26.6)	532.4 (23.8)	1,318.2 (24.2)	
B	39 (1.4)	39 (1.4)	218 (4.0)		42.6 (1.5)	41.7 (1.9)	133.9 (2.5)	
Portal hypertension	206 (7.4)	227 (10.1)	480 (8.8)	0.002	204.5 (7.3)	194.7 (8.7)	391.6 (7.2)	0.126
Tumor size, mm	29.6±23.3	30.4±25.4	34.3±26.8	<0.001	30.6±24.2	30.5±23.7	30.7±24.8	0.972
Multifocal	571 (20.5)	603 (26.9)	1,048 (19.2)	<0.001	618.8 (22.2)	531.9 (23.7)	1,271.7 (23.3)	0.459
Multiple resections	361 (12.9)	437 (19.5)	738 (13.5)	<0.001	419.3 (15.0)	370.0 (16.5)	927.7 (17.0)	0.133
Posterosuperior segments	799 (28.6)	814 (36.3)	1,933 (35.5)	<0.001	881.7 (31.6)	730.7 (32.6)	1,780.6 (32.7)	0.651

Table S1 (continued)

Table S1 (*continued*)

Baseline characteristics	Unweighted cohort				Inverse Probability of Treatment Weighted cohort			
	MV (n=2,792)	HV (n=2,240)	VHV (n=5,447)	P value	MV (n=2,792)	HV (n=2,240)	VHV (n=5,447)	P value
Concomitant other operative procedure (non cholecystectomy)	432 (15.5)	398 (17.8)	853 (15.7)	0.045	433.5 (15.5)	352.7 (15.7)	903.9 (16.6)	0.478
Procedure type				<0.001				0.492
Wedge anterolateral	1,339 (48.0)	1,010 (45.1)	2,155 (39.6)		1,263.1 (45.2)	994.6 (44.4)	2,452.5 (45.0)	
Wedge posterosuperior	753 (27.0)	786 (35.1)	1,883 (34.6)		846.9 (30.3)	704.1 (31.4)	1,750.8 (32.1)	
Left lateral sectionectomy	700 (25.1)	444 (19.8)	1,409 (25.9)		681.9 (24.4)	541.4 (24.2)	1,244.7 (22.9)	
Iwate score (9)				<0.001				0.192
Low	1,112 (39.8)	856 (38.2)	1,639 (30.1)		1066.7 (38.2)	846.3 (37.8)	1,988.6 (36.5)	
Intermediate	1,646 (59.0)	1,319 (58.9)	3,564 (65.4)		1,680.6 (60.2)	1,348.4 (60.2)	3,328.1 (61.1)	
High	33 (1.2)	65 (2.9)	242 (4.4)		43.6 (1.6)	45.3 (2.0)	129.7 (2.4)	
Expert	1 (0.0)	0 (0.0)	2.0 (0.0)		1.2 (0.0)	0 (0.0)	0.6 (0.0)	

Data are presented as mean $\pm$ standard deviation or n (%). CRM, colorectal metastases; HCC, hepatocellular carcinoma; ICC intrahepatic cholangiocarcinoma; IMM, Institute Mutualiste Montsouris.

Table S2 Comparison between perioperative outcomes in IMM grade 1 cases

Perioperative outcomes	Unweighted cohort				Inverse probability of treatment weighted cohort			
	MV (n=2,792)	HV (n=2,240)	VHV (n=5,447)	P value	MV (n=2,792)	HV (n=2,240)	VHV (n=5,447)	P value
Operating time, min	200.7±98.7	213.0±128.1	171.8±95.9	<0.001	204.0±101.5	212.2±136.5	174.8±97.6	<0.001
Blood loss, mL	163.2 (250.8)	164.7 (291.4)	179.9 (294.9)	0.02	168.0 (254.5)	170.9 (315.5)	189.4 (303.8)	0.016
Blood loss (categories), mL				0.10				0.69
<500	2,657 (95.2)	2,111 (94.2)	5,121 (94.0)		2,633.7 (94.3)	2,098.1 (93.7)	5,113.3 (93.9)	
≥500	135 (4.8)	129 (5.8)	326 (6.0)		158.3 (5.7)	141.9 (6.3)	333.7 (6.1)	
Intraoperative blood transfusion	57 (2.0)	41 (1.8)	296 (5.4)	<0.001	65.6 (2.4)	42.9 (1.9)	297.3 (5.5)	<0.001
Pringle maneuver applied	1,108 (40.2)	769 (34.4)	2,583 (48.8)	<0.001	1,176.9 (42.7)	696.6 (31.2)	2,075.7 (39.6)	<0.001
Pringle duration, min	41.5±30.1	41.8±28.0	34.0±23.3	<0.001	43.1±30.6	43.0±29.7	33.9±22.0	<0.001
Open conversion	151±5.4	48±2.1	214±3.9	<0.001	159.4±5.7	40.3±1.8	251.3±4.6	<0.001
Postoperative stay, days	5.1±4.0	6.1±5.9	6.1±5.5	<0.001	5.4±4.3	6.4±6.0	5.5±5.8	<0.001
30-day readmission	79 (2.8)	42 (1.9)	136 (2.5)	0.09	73.1 (2.6)	42.4 (1.9)	183.2 (3.4)	0.01
Postoperative morbidity	416 (14.9)	319 (14.2)	716 (13.1)	0.07	408.0 (14.6)	288.2 (12.9)	795.3 (14.6)	0.18
Major morbidity (Clavien-Dindo grade >2) (18)	123 (4.4)	79 (3.5)	196 (3.6)	0.14	119.5 (4.3)	75.7 (3.4)	274.1 (5.0)	0.02
Reoperation	28 (1.0)	22 (1.0)	48 (0.9)	0.84	26.5 (1.0)	21.3 (1.0)	73.7 (1.4)	0.25
30-day mortality	7 (0.3)	6 (0.3)	12 (0.2)	0.92	8.8 (0.3)	5.1 (0.2)	15.8 (0.3)	0.87
In-hospital mortality	8 (0.3)	8 (0.4)	15 (0.3)	0.83	9.7 (0.3)	7.3 (0.3)	17.1 (0.3)	0.98
90-day mortality	9 (0.3)	9 (0.4)	20 (0.4)	0.89	10.4 (0.4)	7.7 (0.3)	23.7 (0.4)	0.86
Close/involved margins (≤1 mm) for malignancies	375 (13.6)	437 (19.6)	948 (17.5)	<0.001	375.2 (13.6)	41.7 (18.5)	1,053.8 (19.6)	<0.001

Data are presented as mean ± standard deviation or n (%).